could be obtained by shortening the duration of OC administration. No interferences with hemostatic balance are documented.

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Waldenstrom's Macroglobulinemia Transformed Into Immunoblastic Lymphoma Presenting With Malignant Ascites

To the Editor: On rare occasions, Waldenstrom's macroglobulinemia (WM) may transform into immunoblastic lymphoma (IL), a phenomenon analogous to Richter's syndrome occurring with chronic lymphocytic leukemia [1]. Transformation is signaled by diffuse lymphadenopathy, fevers, night sweats, and weight loss [2]. To our knowledge, we report the first case of a patient with malignant ascites as a presenting manifestation of WM that transformed into IL.

A 57-year-old male with a history of WM presented with 2 weeks of progressive abdominal distention, cervical adenopathy, fevers, night sweats, and weight loss. Ten years previously, he was diagnosed with WM. Immunocytochemistry of a marrow specimen demonstrated the majority of cells to be IgM kappa-positive. He received multiple agents, including cyclophosphamide, vincristine, prednisone, and chlorambucil. He had no history of ethanol use or liver disease.

Physical examination revealed left-sided cervical, supraclavicular, and axillary adenopathy. The abdomen was distended with shifting dullness. Serum lactate dehydrogenase (LDH) was 1,817 units/l and plasma viscosity was 2.87 (nl 0.99–1.55). White blood cell count was 24,000 cells/mm^3 with 30% immunoblasts, suggesting transformation of WM into a more aggressive neoplasm. Flow cytometry of these cells was consistent with WM. Paracentesis revealed numerous cells similar in morphology to the immunoblasts in the peripheral blood (Fig. 1); the culture was sterile. Ultrasound of the liver was normal. Computerized tomography scan showed massive thoracic and abdominal lymphadenopathy. A cervical lymph node biopsy was consistent with IL and stained positive for IgM kappa, supporting clonal transformation. The patient denied further intervention and died 13 days after admission.

Transformation of WM into IL is a rare event, occurring in approximately 1.7% of cases of WM [3]. The mean survival once transformation occurs in 2 months [2]. Prior therapy with alkylating agents may predispose to transformation, though this remains to be proven [3]. IL is characterized by the monomorphous proliferation of immunoblasts, which are large cells with plasmacytoid features [1]. Both WM and IL are clonal diseases, and the change in histologic appearance of the cells characteristic of WM into the larger cells of IL is believed to represent evolution of the same clone of cells. Furthermore, the appearance of identical heavy and light chains on both tumor cell types supports clonal evolution [4].

Ascites due to IL is very rare. Peritoneal lymphomatosis is much less common than peritoneal carcinomatosis and carries a dismal prognosis [5]. Runyon and Hoefs [5] reported on three patients with malignant ascites as

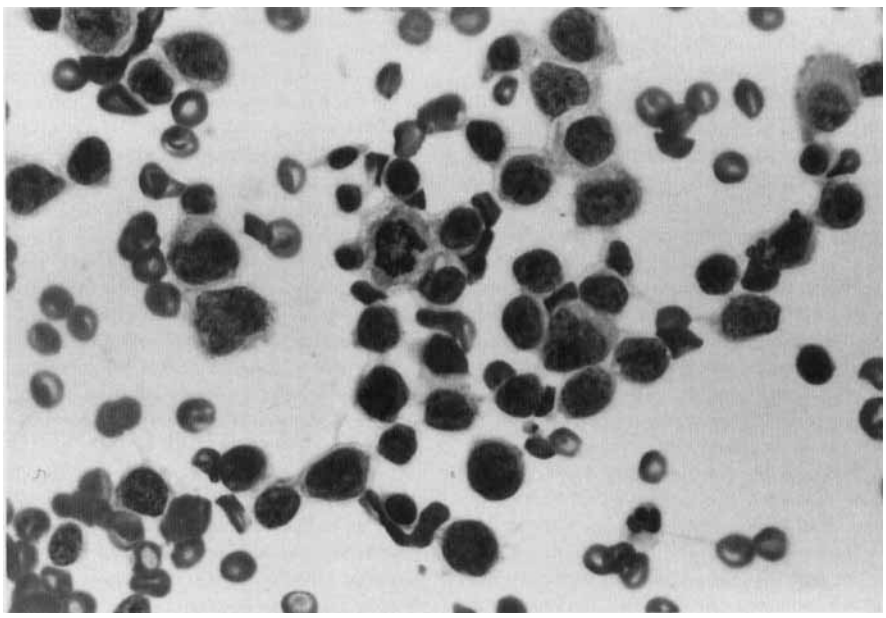

Fig. 1. Peritoneal fluid positive for immunoblastic lymphoma. Note mitotic figure in the center. Papanicalou cytocentrifuge preparation, magnification × 100, oil.

a manifestation of lymphoma, and all died before receiving chemotherapy. If a patient with WM develops ascites, clinicians should consider the possibility that the disease has transformed into IL, especially if the patient has received alkylating agents.

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Acute Leg Ischaemia as a Presentation of Hyperleukocytosis Syndrome in Acute Myeloid Leukaemia

To the Editor: Recently, Campbell and Mitchell [1] reported the first case of acute leg ischaemia as a presentation of hyperleukocytosis syndrome in acute myeloid leukaemia (AML). We present a similar case in a patient without previous clinical ischaemia.

In 1985 a 42-year-old smoker was admitted for pain in his right leg which had lasted 2 days. Examination revealed absent tibial and pedal pulses. Full blood examination revealed haemoglobin 9.8 g/dl, platelets 30×10^9/l, white cell count (WCC) 150×10^9/l (95% blasts). The coagulation study was normal. Bone marrow examination confirmed the diagnosis of AML-M2. Angiography demonstrated thrombosis on the second sector of the right popliteal artery. Arterial thrombolysis with streptokinase was performed without success, and a cytoreduction with hydroxyurea (8 g/day) was later performed. Following the hydroxyurea therapy, WCC dropped to 60×109/l. After three thrombectomies in 6 days, with subsequent stenosis in all cases, treatment with cytosine arabinoside, daunorubicin, and thioguanine was begun; in spite of this, necrotic signs in the right leg were evident and right supracondylar amputation was decided upon. After standard chemotherapy for AML complete remission was reached. Two years later a bone marrow transplant was performed, but the patient died on day 17 following the transplant, as a consequence of a diffuse alveolar haemorrhage that was confirmed in the postmortem examination.

The presence of arterial leukocyte thrombi was clearly demonstrated in the autopsy analysis, especially in a patient affected by AML with affectation fundamentally at the level of small calibre vessels [2]. This association is more evident when hyperleukocytosis [3] or previous arterial damage [4] exist. Though major vessel obstructions are uncommon, we believe that this is probably based on underestimates; our case data of 1985 and the reading of the Campbell and Mitchell case [1] encouraged us to revise our file of leukaemias, which induced us to think that unpublished cases could exist. Campbell and Mitchell propose that developed hyperleukocytosis produced leukostasis at the site of an atherosclerotic stenosis. We report the second case of peripheral arterial thrombosis where the age of the patient, the absence of symptoms and signs, and the nonappearance of atherosclerosis in the autopsy lead us to believe that the increase in the secondary sanguine viscosity to the hyperleukocytosis was sufficient to produce vascular occlusion.

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Simultaneous Occurrence of Lupus Anticoagulant, Factor VIII Inhibitor and Localized Pemphigoid

To the Editor: Acquired hemophilia, a rare disorder, has been observed in association with various autoimmune diseases [1]. Among them, bullous skin lesions have been reported, but rarely bullous pemphigoid (BP) [2]. Lupus anticoagulant (LA) is also encountered in many clinical states characterized by immunologic disorders [3]. Herein, we describe a case of localized pemphigoid associated with both LA and factor VIII inhibitor. To our knowledge, this combination has not yet been reported.

A 92-year-old woman, 2 weeks after apparition of a bullous dermatosis on the left leg, developed a large ecchymosis over the upper extremities and abdomen. She had no family or past history of a bleeding disorder. Histological and immunofluorescence studies confirmed the diagnosis of BP. Blood cell count, platelet count, and prothrombin time were within normal ranges. Activated partial thromboplastin time (APTT) was prolonged (102 sec; control value: 34 sec). The addition of normal plasma (1:1) failed to correct the APTT, leading us to suspect an acquired anticoagulant. The presence of LA was confirmed by a neutralization procedure using hexagonal (II) phase phosphatidylethanol (Staclot LA, Diagnostica Stago, Asnieres, France). The severity of bleeding prompted us to suspect an associated clotting factor deficiency. Fibrinogen factors II, V, IX, XI, and XII were within normal ranges, but factor VIII level was 2%. The presence of a factor VIII inhibitor was confirmed using the Bethesda method [4]. An antihuman factor VIII inhibitor of 32 Bethesda units (BU) was identified while the titer of antiporcine VIII inhibitor activity was 2 BU. Antinuclear antibodies, antidouble-stranded DNA antibodies, and anticardiolipin antibodies were not detected.

Acute bleeding was controlled using porcine VIIIC: HyateC (Speywood, Berkshire, UK) at 50 U/kg, three times a day. No recurrent bleeding was observed during the hospitalization. Treatment was disrupted after 3 days, while a prednisolone therapy (1 mg/kg/day) was initiated. After 2 weeks of steroid therapy, dermatological lesions disappeared, while biological abnormalities were less pronounced: factor VIII increased to 15%, with an